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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/620,052	07/14/2003	Yasumichi Hitoshi	021044-004010US	7655

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EXAMINER

HALVORSON, MARK

ART UNIT	PAPER NUMBER
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1642

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/21/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No. 10/620,052	Applicant(s) HITOSHI ET AL.	
	Examiner Mark Halvorson	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 1/8/2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-22 is/are pending in the application.
- 4a) Of the above claim(s) 3-6, 10, 13, 14, 17 and 19-22 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 7-9, 11, 12, 15, 16 and 18 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>1/8/2007</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-22 are pending.

Claim 3-6, 10, 13, 14, 17 and 19-22 have been withdrawn.

Claims 1, 2, 7-9, 11, 12, 15, 16 and 18 are under currently under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

- 35 USC § 112 2nd paragraph rejection withdrawn

The rejection of claims 1, 3, 7-9, 11, 12, 15, 16 and 18 for being indefinite is withdrawn in view of the amendments to claim 1.

35 USC § 112 1st paragraph rejection withdrawn

The rejection of claims 1, 3, 7-9, 11, 12, 15, 16 and 18 for failing to comply with the written description requirement is withdrawn in view of the of the amendments to claim 1.

35 USC § 102(b) rejections maintained

The rejection of claims 1, 7, 8, 15, 16, and 18 under 35 USC § 102(b) as being anticipated by Harrington et al is maintained.

Applicants argue that Harrington et al does not disclose all the elements of the claims as amended. Specifically, Applicants argue that Harrington et al does not disclose determination of the effect of a compound upon a heterologous FEN1 protein.

Applicant's arguments have been fully considered but they are not persuasive. Harrington et al discloses that the term FEN-1 polypeptide includes fusion proteins or analogs of FEN-1 (column 15, lines 53-59). Thus, FEN-1 polypeptide comprises heterologous proteins. Furthermore, Harrington et al disclose recombinant FEN-1 polypeptides (column 18, lines 47-50) as well as FEN-1 polypeptides encoded by FEN-1 transgenes (column 28, lines 11-15).

35 USC § 102(b) rejections withdrawn

The rejection of claims 1, 9, 11 and 12 under 35 USC § 102(b) as being anticipated by Bai et al is withdrawn in view of Applicants amendment to claim 1.

NEW REJECTIONS: Based on the Amendment

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 9, 11, and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Harrington et al (US Patent No: 5, 874, 283, issued February 23, 1999).

The claims are drawn to a method for identifying a compound that modulates cell cycle arrest, the method comprising contacting a cell comprising a target compound consisting of a flap structure specific endonuclease 1 (FEN1) and determining the chemical or phenotypic effect of the compound upon the cell, thereby identifying a compound that modulates cell cycle arrest, wherein the cell is the transformed cancer cell line A549.

Prior art was not found on a method for identifying a compound that modulates cell cycle arrest, wherein the cell is the transformed cancer cell line A549. Thus, a search was carried out on one of the other species of transformed cell lines, Hela cells.

Harrington et al disclose a method for identifying modulating agents of the FEN-1 peptide of SEQ ID NO:14 (see Sequence Search) which reduce the cell's capacity to repair DNA damage or inhibit endogenously naturally-occurring FEN1 (column 39 lines 25-28).

Harrington et al further disclose that the present invention may be used to design drugs that inhibit the binding of FEN1 to DNA flaps or nicks and to catalyze nuclease

Art Unit: 1642

activity on the flap strand (column 42 lines 58-61). The nucleic acid of SEQ ID NO:13 encodes the peptide of SEQ ID NO:14.

In addition Harrington et al teach a recombinant FEN1 polypeptide used in a yeast two hybrid system to detect compounds that bind to FEN1 to identify candidate FEN-1 modulatory agents. (column 36 line 62 to column 39 line 24). Enzymatic activity is used to detect binding of a compound to FEN1 (Id).

Harrington et al also discloses a method of expressing FEN1 in HeLa cells, a transformed cell line.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Harrington et al as applied to claim 1 above, and further in view of Shibata et al (IDS, January 2002).

Claim 2 is drawn to method for identifying a compound that modulates cell cycle arrest, the method comprising contacting a cell comprising a target compound consisting of a flap structure specific endonuclease 1 (FEN1) and determining the chemical or phenotypic effect of the compound upon the cell, thereby identifying a compound that modulates cell cycle arrest, wherein the cell cycle effect of the compound is compared to the effect of the compound on a cell comprising a dominant negative mutant FEN1 polypeptide.

Harrington et al disclose a method for identifying modulating agents of the FEN-1 peptide of SEQ ID NO:14 (see Sequence Search) which reduce the cell's capacity to repair DNA damage or inhibit endogenously naturally-occurring FEN1 (column 39 lines 25-28). These modulating agent are candidate neoplastic agents which can be tested further for antineoplastic activity. Harrington et al further disclose that the present invention may be used to design drugs that inhibit the binding of FEN1 to DNA flaps or nicks and to catalyze nuclease activity on the flap strand (column 42 lines 58-61). The nucleic acid of SEQ ID NO:13 encodes the peptide of SEQ ID NO:14.

In addition Harrington et al teach a recombinant FEN1 polypeptide used in a yeast two hybrid system to detect compounds that bind to FEN1 to identify candidate FEN-1 modulatory agents. (column 36 line 62 to column 39 line 24). Enzymatic activity is used to detect binding of a compound to FIN1 (Id).

Harrington et al does not specifically teach dominant negative mutant FEN1 polypeptides.

Shibata et al teach that expression of dominant negative FEN1 mutants results in the alteration of cell cycle checkpoint protein levels.

One of ordinary skill in the art would have been motivated to apply Shibata et al's negative FEN1 mutant proteins to Harrington et al's method for identifying a compound that modulates cell cycle arrest because Harrington et al describes FEN-1 mutants wherein the native protein has at least one amino acid deleted or replaced by another amino acid and the mutants exhibiting altered biological activity (column 32, lines 5-9).

It would have been prima facie obvious to one skilled in the art to have combined Shibata et al's negative FEN1 mutant proteins with Harrington et al's method for

Art Unit: 1642

identifying a compound that modulates cell cycle arrest to determine the effect of the compound upon FEN1 dependent cell proliferation.

Summary

Claims 1, 2, 7-9, 11, 12, 15, 16 and 18 stand rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Halvorson, PhD whose telephone number is (571) 272-6539. The examiner can normally be reached on Monday through Friday from 8:30am to 5 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley, can be reached at (571) 272-0898. The fax phone number for this Art Unit is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

Art Unit: 1642

For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mark Halvorson, PhD
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